

Posters

4. New therapies

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73 Influence of treatment with sildenafil on lung function and exercise tolerance in cystic fibrosis adults

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Objectives: Phosphodiesterase 5 inhibitors (IPDE5) are able to restore chloride transport in F508del cystic fibrosis (CF) airway epithelium. CF patients with severe lung disease are at risk of pulmonary hypertension and impaired exercise tolerance. Treatment with IPDE5 is a promising strategy in CF.

Methods: We conducted a study in 12 stable F508del homozygous CF adults (5 males and 7 females) with median (IQR) age of 25.9 (22.8–27.6) years without *Burkholderia cepacia* complex airway colonization. We administered sildenafil for 30 days and evaluated pulmonary function, respiratory symptoms and exercise tolerance before and after treatment using spirometry (forced expiratory volume in 1 sec. [FEV₁]), 6-minute walking test (6-minute walking distance [6-MWD]) and CFQ-R quality of life questionnaire (physical and respiratory domain [PHYS and RESP, respectively]). 8 patients completed the study (2 dropped due to pulmonary exacerbation and further 2 due to headaches). Exercise tolerance changed significantly (median and IQR; Wilcoxon test): 6-MWD 618 (612–692) vs. 577 (562–633) m, $p=0.012$, and PHYS 93.8 (68.8–100.0) vs. 89.6 (60.4–97.9), $p=0.043$, whereas pulmonary function and respiratory symptoms did not. Transient headaches were common adverse events during the first 1–2 weeks of sildenafil treatment in 7 of the 12 patients.

Conclusion: We conclude that short-term sildenafil treatment in CF adults led to an improvement of exercise tolerance without changing pulmonary function and respiratory symptoms.

Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00064203 (University Hospital Motol, Prague, Czech Republic).

75 Modulation of *Burkholderia cenocepacia* virulence factors and biofilm formation by liposomal tobramycin-bismuth

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Objectives: *Burkholderia cenocepacia* is an opportunistic pathogen that causes severe infections in patients with cystic fibrosis. This bacterium is intrinsically resistant to most antibiotics. Tobramycin have demonstrated an inhibitory effect on *B. cenocepacia* although resistance can develop over time. Bismuth thiols have been shown to have a broad spectrum of activities against *B. cenocepacia*. In order to improve the efficacy of the bismuth thiols in combination with tobramycin, the dual entrapment of these agents into liposomes was performed.

Methods: Formulations of liposomal tobramycin and bismuth (LTob-BiEDT) were prepared and their ability to reduce biofilm development and secretion of virulence factors (protease and lipase) were determined. It was found that LTob-BiEDT was more effective (2-fold) at reducing and preventing biofilm development than FTob-BiEDT at sub-inhibitory concentrations. LTob-BiEDT also inhibited the secretion of the virulence factor lipase much more (20-fold) successfully than FTob-BiEDT although neither formulation showed any inhibitory effect on secretion of the virulence factor protease.

Conclusion: Sub-inhibitory concentrations of LTob-BiEDT are capable of reducing and preventing biofilm development and secretion of some virulence factors in *B. cenocepacia*. The liposomal management of experimental *B. cenocepacia* in animal models is in progress.

74 Improved tolerability, adherence and reduced intravenous (IV) antibiotic usage in CF patients receiving inhaled versus nebulised antibiotic prophylaxis. A real world comparison of tobramycin inhaled powder (TIP) and tobramycin inhaled solution (TIS)

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Objectives: Studies have documented poor real-life adherence to nebulised antibiotic therapy. Recent availability of inhaled antibiotics offers potential new therapeutic strategies. No data exists on real-life experience with inhaled antibiotics.

Methods: Consecutive adult CF patients commencing inhaled antibiotic therapy (TIP) were recruited at our centre from November 2011 to November 2012. A questionnaire, at time of recruitment, recorded safety, tolerability, efficacy and adherence scores relating to original nebulised treatment (TIS), with repeat measures planned at 3, 6, 9 and 12 months to evaluate new inhaled therapy (TIP).

Conclusion: 76 patients were enrolled. 1 patient died (unrelated to the drug). 1 patient received a lung transplant. 10.5% (n=8) were intolerant of TIS prior to enrolment, with 62% (5/8) subsequently tolerating TIP. In total, 9% (7/74) discontinued TIP; 6 due to cough/bronchospasm and 1 due to oral candidiasis. Based on last observation carried forward, there was a significant increase in mean adherence score from 2.1 in the TIS group to 2.9 in the TIP group ($p=0.001$). In a subgroup analysis of patients completing 9 months on TIP there was a significant reduction in the number of IV antibiotic courses received compared with TIS ($p=0.017$). There was no significant difference in cough, lung function, or adverse events between the groups. We demonstrate improved tolerability and adherence, reduced IV antibiotic usage and stable lung function with inhaled versus nebulised antibiotic therapy. Subgroup analysis supports a trial of inhaled antibiotics in those who fail nebulised treatment.

No industry funding was provided for this study.